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EXAMINER

TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 05/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/848,727

Applicant(s)

GAU, VINCENT JEN-JR.

Examiner

MY-CHAU T. TRAN

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 83-95,98-104,108,112-118 and 120-130 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 83-95,98-104,108,112-118 and 120-130 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 November 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/6/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/06/2006 has been entered.

Application and Claims Status

2. Applicant's amendment and response filed 03/06/2006 are acknowledged and entered. Claims 83, 124, 125, and 127 have been amended. Claims 128-130 have been added.

3. The amendment filed on 09/12/2005: cancelled claim 119; amended claims 83 and 120; and added claims 124-127. The amendment filed on 12/17/2004: cancelled claims 96, 97, 105-107, and 109-111; amended claims 83-86, 95, 98, 102-104, 108, and 112; and added claims 114-123. The amendment filed on 06/28/2004: cancelled claims 1-20, 51-52, and 75-82; and added claims 83-113. The amendment filed on 11/13/2003: cancelled claims 75-82; and added claims 75-82. The amendment filed on 05/05/2003: cancelled claims 21-50; amended claims 1, 3-20; and added claims 51-74.

4. Claims 83-95, 98-104, 108, 112-118, and 120-130 are pending.

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5. Claims 83-95, 98-104, 108, 112-118, and 120-130 are under consideration in this Office Action.

Priority

6. This instant application claims benefit to a provisional application of 60/201,603 filed 05/03/2000. This instant application is granted the benefit of priority for 60/201,603 under 35 U.S.C 119(e).

Claim Objections

7. Claim 123 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 123 recite “*the method of claim 83 further comprising employing the potential to determine the presence or quantity of the target analyte in the sample*”. However, claim 83 recite the method step of ‘*conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode... wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode*’, which is analogous to the limitation recited in claim 123, i.e. a potential need to be utilize to “*cause a redox reaction between a component in the sample and the working electrode*” as claimed would be analogous to the limitation of ‘*employing the potential to determine the presence or quantity of the target analyte in the sample*’. Therefore, claim 123 fail to further limit the subject matter of claim 83.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 83, 126, 127, and 130 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 83 recites the method of detecting the presence or measuring the quantity of a target analyte in a sample reagent. The method comprises the step of 1) positioning the sample on a sensor; 2) conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode while measuring a current flowing through the working electrode wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode, and the current through the working electrode is balanced by a current through the counter electrode; and 3) employing the measured current to determine the presence or quantity of a target analyte in the sample.

The sensor structurally comprises a working electrode, a reference electrode, and a counter electrode on a substrate, and a self-assembly monolayer on at least one of the electrodes. The reference electrode structurally consists of a single layer of an electrically conductive material. The molecules in the self-assembly monolayer includes a sulfur that is bonded directly to the at least one electrode, i.e. newly added limitation.

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Claims 126 and 127 recite that the self-assembly monolayer is positioned on the working electrode, the reference electrode, and the counter electrode.

Claim 130 recites that the self-assembly monolayer is positioned on the reference electrode.

The recitation that the sulfur containing self-assembly monolayer is directly bonded to all three electrodes, i.e. the working electrode, the reference electrode, and the counter electrode, in regard to claims 83, 126, and 127 has no clear support in the specification and the claims as originally filed. And the recitation that the sulfur containing self-assembly monolayer is directly bonded to only the reference electrode in regard to claims 83 and 130 has no clear support in the specification and the claims as originally filed.

The instant specification disclosed that the surface of the working electrode is modify using self-assembly monolayer for anchoring macromolecules (page 10, paragraph [064], page 11, paragraph [067], page 14, paragraph [078]) and specifically the sulfur containing self-assembly monolayer is use to modify gold working electrode (page 10, paragraph [0139]). These disclosures are not support for the recitation that the sulfur containing self-assembly monolayer is directly bonded to all three electrodes, i.e. the working electrode, the reference electrode, and the counter electrode, in regard to claims 83, 126, and 127 and the recitation that the sulfur containing self-assembly monolayer is directly bonded to only the reference electrode in regard to claims 83 and 130. Consequently, the scope of the invention as originally disclosed in the specification would not encompass the scope of the limitations of claims 83, 126, 127, and 130, since there is no specification support or original claim support for such scope; nor has applicant provided any indication where such support exists.

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Accordingly, the recitation that the sulfur containing self-assembly monolayer is directly bonded to all three electrodes, i.e. the working electrode, the reference electrode, and the counter electrode, in regard to claims 83, 126, and 127 and the recitation that the sulfur containing self-assembly monolayer is directly bonded to only the reference electrode in regard to claims 83 and 130 are considered new matters.

If applicant believes the rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP § 714.02 and 2163.06.

10. *The instant invention recites the method of detecting the presence or measuring the quantity of a target analyte in a sample reagent.*

The method comprises the step of 1) positioning the sample on a sensor; 2) conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode while measuring a current flowing through the working electrode wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode, and the current through the working electrode is balanced by a current through the counter electrode; and 3) employing the measured current to determine the presence or quantity of a target analyte in the sample.

The sensor structurally comprises a working electrode, a reference electrode, and a counter electrode on a substrate, and a self-assembly monolayer on at least one of the electrodes.

The reference electrode structurally consists of a single layer of an electrically conductive material.

The molecules in the self-assembly monolayer includes a sulfur that is bonded directly to the at least one electrode.

The method step of conducting an analysis is interpreted as controlling the potential difference between the counter electrode and the working electrode.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Wink et al. (*The Analyst*, 1997, 122(4), pgs. 43R-50R).

Choong et al. disclose an apparatus and methods for detecting single base extension to an oligonucleotide using electrochemical redox labels (see e.g. Abstract; col. 1, lines 7-16; col. 3, lines 25-31; col. 9, lines 17-22).

The apparatus comprises a supporting substrate, a plurality of first electrode (refers to instant claimed working electrode), a counter electrode, and a reference electrode wherein the first electrode is in contact with a supporting substrate and oligonucleotide probes are immobilized on the first electrode via a polymer (see e.g. col. 5, line 15 thru col. 6, line 41; col. 7, lines 30-40). The substrate comprises materials such as silicon, glass, plastic, and ceramic (refers to instant claim 87) (see e.g. col. 5, lines 54-58). The substrate has a surface area of between $0.01 \mu\text{m}^2$ and 5 cm^2 (refers to instant claim 113)(see e.g. col. 6, lines 12-26). The first electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3). The counter electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3; col. 7, lines 29-40). The reference electrode comprises materials such as silver wire (refers to instant claimed limitation of “*the reference electrode consists of a single*

layer of an electrically conductive material", and claims 101 and 118). Additionally, the electrodes are connected to a power source and a means for controlling the power source.

The method comprises a) contacting the sample to the plurality of first electrodes, b) adding the reagent comprising the electrochemical redox labels, c) detecting the presence of the electrochemical redox labels to identify the base extension (see e.g. col. 4, lines 39-53; col. 8, lines 9-35; col. 10, lines 10-41). The detection step includes controlling the current flow between two electrodes (see e.g. col. 7, lines 41-50; col. 17-30). The detection method includes amperometric and cyclic voltammetry (refers to instant claims 114-117) (see e.g. col. 4, lines 5-14; col. 10, lines 10-41). In addition, Choong et al. disclose the step of forming the polymer onto the working electrode (see e.g. col. 11, lines 31-40).

The apparatus of Choong et al. differs from the presently claimed invention by failing to disclose sulfur containing self-assembled monolayer.

Wink et al. disclose self-assembled monolayers (SAMs) and the methods of making and using the SAMs (see e.g. Abstract; pg. 43R, right col., lines 16-37). The class of monolayers includes disulfides (R-S-S-R), sulfides (R-S-R) and thiols (R-SH) that have a strong adsorption on a metal surface (see e.g. pg. 43R, right col., lines 26-29; pg. 44R, left col., lines 12-19). The SAMs modify sensor surface can be use in application such as electrochemical and surface plasmon resonance (see e.g. pg. 45R, right col., line 1 thru pg. 48R, left col., line 2). In electrochemical application, SAMs is use to immobilize biological molecules such as enzymes and DNA sequences (see e.g. pg. 46R, left col. line 5 thru right col., line 23). SAMs provide a stable monolayer from dilute solutions and ensuring a uniform immobilization (see e.g. pg. 45R, right col., lines 7-9).

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It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose sulfur containing self-assembled monolayer as taught by Wink et al. in the apparatus of Choong et al. One of ordinary skill in the art would have been motivated to disclose sulfur containing self-assembled monolayer in the apparatus of Choong et al. for the advantage of providing a stable monolayer from dilute solutions and ensuring a uniform immobilization (Wink: pg. 45R, right col., lines 7-9) since both Choong et al. and Wink et al. disclose immobilization of DNA sequences onto a metal surface (Choong: col. 11, lines 31-40; Wink: pg. 46R, right col., lines 15-23). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al. and Wink et al. because Wink et al. disclose the success of immobilization of DNA sequences onto a metal surface via sulfur containing self-assembled monolayer (Wink: pg. 46R, right col., lines 15-23).

Therefore, the combine teachings of Choong et al. and Wink et al. do render the apparatus and method of the instant claims *prima facie* obvious.

13. Claims 84, 91, and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Wink et al. (*The Analyst*, 1997, 122(4), pgs. 43R-50R) as applied to claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129, and further in view of Cozzette et al. (US Patent 5,200,051) alone or as evidenced by Heller et al. (US Patent 5,403,700) regarding chromium as another type of metal-substrate adhesive.

Choong et al. disclose an apparatus and methods for detecting single base extension to an oligonucleotide using electrochemical redox labels (see e.g. Abstract; col. 1, lines 7-16; col. 3, lines 25-31; col. 9, lines 17-22).

The apparatus comprises a supporting substrate, a plurality of first electrode (refers to instant claimed working electrode), a counter electrode, and a reference electrode wherein the first electrode is in contact with a supporting substrate and oligonucleotide probes are immobilized on the first electrode via a polymer (see e.g. col. 5, line 15 thru col. 6, line 41; col. 7, lines 30-40). The substrate comprises materials such as silicon, glass, plastic, and ceramic (refers to instant claim 87) (see e.g. col. 5, lines 54-58). The substrate has a surface area of between $0.01 \mu\text{m}^2$ and 5 cm^2 (refers to instant claim 113)(see e.g. col. 6, lines 12-26). The first electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3). The counter electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3; col. 7, lines 29-40). The reference electrode comprises materials such as silver wire (refers to instant claimed limitation of "*the reference electrode consists of a single layer of an electrically conductive material*", and claims 101 and 118). Additionally, the electrodes are connected to a power source and a means for controlling the power source.

The method comprises a) contacting the sample to the plurality of first electrodes, b) adding the reagent comprising the electrochemical redox labels, c) detecting the presence of the electrochemical redox labels to identify the base extension (see e.g. col. 4, lines 39-53; col. 8, lines 9-35; col. 10, lines 10-41). The detection step includes controlling the current flow between two electrodes (see e.g. col. 7, lines 41-50; col. 17-30). The detection method includes amperometric and cyclic voltammetry (refers to instant claims 114-117) (see e.g. col. 4, lines 5-14; col. 10, lines 10-41). In addition, Choong et al. disclose the step of forming the polymer onto the working electrode (see e.g. col. 11, lines 31-40).

Wink et al. disclose self-assembled monolayers (SAMs) and the methods of making and using the SAMs (see e.g. Abstract; pg. 43R, right col., lines 16-37). The class of monolayers includes disulfides (R-S-S-R), sulfides (R-S-R) and thiols (R-SH) that have a strong adsorption on a metal surface (see e.g. pg. 43R, right col., lines 26-29; pg. 44R, left col., lines 12-19). The SAMs modify sensor surface can be use in application such as electrochemical and surface plasmon resonance (see e.g. pg. 45R, right col., line 1 thru pg. 48R, left col., line 2). In electrochemical application, SAMs is use to immobilize biological molecules such as enzymes and DNA sequences (see e.g. pg. 46R, left col. line 5 thru right col., line 23). SAMs provide a stable monolayer from dilute solutions and ensuring a uniform immobilization (see e.g. pg. 45R, right col., lines 7-9).

The combine teaching of Choong et al. and Wink et al. are obvious over the instant claimed method because one of ordinary skill in the art would have been motivated to disclose sulfur containing self-assembled monolayer in the apparatus of Choong et al. for the advantage of providing a stable monolayer from dilute solutions and ensuring a uniform immobilization (Wink: pg. 45R, right col., lines 7-9). However, the combine teachings of Choong et al. and Wink et al. differ from the presently claimed invention by failing to disclose an adhesive underneath each of the electrodes.

Cozzette et al. disclose a biosensor and various methods for using the biosensor (see e.g. Abstract; col. 1, lines 17-64; col. 11, line 49 to col. 12, line 25). In general, the method disclosed is the method of electrochemically detecting the changes in concentration of electroactive species that result from the reaction between the enzyme and the substrate with the biosensor (see e.g. col. 12, lines 7-25; col. 20, line 4 to col. 21, line 51; fig. 14). In general, the biosensor comprises

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a planar substrate and a base sensor that includes a unit cell that comprises an indicator electrode and a combined reference and counter electrode and an additional structure of a permaselective layer (see e.g. col. 12, lines 26-44; col. 24, lines 23-42; col. 26 line 36 thru col. 29, line 56; col. 56, lines 16-25; fig. 1, 4, and 12). The substrate comprises material such as silicon, glass, or plastic (see e.g. col. 24, lines 7-11; col. 25, lines 36-44). The electrode comprises material such as gold or platinum (e.g. col. 24, line 61 thru col. 25, line 8). A metal-substrate adhesive comprises a titanium layer (see e.g. col. 25, lines 55-61). Although Cozzette et al. disclose titanium as a metal-substrate adhesive, other type of metal-substrate adhesive are known such as chromium as evidence by Heller et al. wherein the adhesive layer include compounds such as chromium or titanium (col. 6, lines 54-68 to col. 7, lines 1-4). The electrochemical detection means includes amperometric, potentiometric, or conductimetric (see e.g. col. 19, lines 31-35). Additionally, the unit cell is well in a microplate (see e.g. fig. 1, 4, and 12). One type of biosensor disclosed by Cozzette et al. is a glucose sensor and the method of detecting the concentration of the glucose in the sample by measuring the current generated as the result of the electrochemical reaction (see e.g. col. 22, lines 34-67; col. 23, lines 35-40; col. 43, lines 31-68). The method comprises the step of applying the appropriate potential across the indicator electrode, with respect to the reference electrode, that result in the consumption of the electroactive species and the production of a measurable current (see e.g. col. 22, lines 34-67).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose an adhesive underneath each of the electrodes as taught by Cozzette et al. in the apparatus of Choong et al. and Wink et al. One of ordinary skill in the art would have been motivated to disclose an adhesive underneath each of the electrodes in the

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apparatus of Choong et al. and Wink et al. for the advantage of a) providing a layer that act as a barrier against interfering chemical species while allowing the transport of smaller detectable chemical moieties of transport (Cozzette: col. 12, lines 32-34) and b) providing an adhesive layer that promotes the adhesion the metal layer onto the substrate surface (Cozzette: col. 25, lines 58-61) since both Choong et al. and Cozzette et al. disclose a biosensor comprising three electrode system (Choong: col. 5, lines 37-44; Cozzette: col. 12, lines 26-44). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al., Wink et al., and Cozzette et al. because Cozzette et al. disclose the success via examples of a biosensor comprising an adhesive layer underneath each of the electrodes (Cozzette: col. 68, line 40 thru col. 69, line 63).

Therefore, the combine teachings of Choong et al., Wink et al., and Cozzette et al. do render the apparatus and method of the instant claims *prima facie* obvious.

14. Claims 93, 102, 121, and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Wink et al. (*The Analyst*, 1997, 122(4), pgs. 43R-50R) as applied to claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129, and further in view of Weetall (US Patent 4,963,245).

Choong et al. disclose an apparatus and methods for detecting single base extension to an oligonucleotide using electrochemical redox labels (see e.g. Abstract; col. 1, lines 7-16; col. 3, lines 25-31; col. 9, lines 17-22).

The apparatus comprises a supporting substrate, a plurality of first electrode (refers to instant claimed working electrode), a counter electrode, and a reference electrode wherein the

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first electrode is in contact with a supporting substrate and oligonucleotide probes are immobilized on the first electrode via a polymer (see e.g. col. 5, line 15 thru col. 6, line 41; col. 7, lines 30-40). The substrate comprises materials such as silicon, glass, plastic, and ceramic (refers to instant claim 87) (see e.g. col. 5, lines 54-58). The substrate has a surface area of between $0.01 \mu\text{m}^2$ and 5 cm^2 (refers to instant claim 113)(see e.g. col. 6, lines 12-26). The first electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3). The counter electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3; col. 7, lines 29-40). The reference electrode comprises materials such as silver wire (refers to instant claimed limitation of “*the reference electrode consists of a single layer of an electrically conductive material*”, and claims 101 and 118). Additionally, the electrodes are connected to a power source and a means for controlling the power source.

The method comprises a) contacting the sample to the plurality of first electrodes, b) adding the reagent comprising the electrochemical redox labels, c) detecting the presence of the electrochemical redox labels to identify the base extension (see e.g. col. 4, lines 39-53; col. 8, lines 9-35; col. 10, lines 10-41). The detection step includes controlling the current flow between two electrodes (see e.g. col. 7, lines 41-50; col. 17-30). The detection method includes amperometric and cyclic voltammetry (refers to instant claims 114-117) (see e.g. col. 4, lines 5-14; col. 10, lines 10-41). In addition, Choong et al. disclose the step of forming the polymer onto the working electrode (see e.g. col. 11, lines 31-40).

Wink et al. disclose self-assembled monolayers (SAMs) and the methods of making and using the SAMs (see e.g. Abstract; pg. 43R, right col., lines 16-37). The class of monolayers

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includes disulfides (R-S-S-R), sulfides (R-S-R) and thiols (R-SH) that have a strong adsorption on a metal surface (see e.g. pg. 43R, right col., lines 26-29; pg. 44R, left col., lines 12-19). The SAMs modify sensor surface can be use in application such as electrochemical and surface plasmon resonance (see e.g. pg. 45R, right col., line 1 thru pg. 48R, left col., line 2). In electrochemical application, SAMs is use to immobilize biological molecules such as enzymes and DNA sequences (see e.g. pg. 46R, left col. line 5 thru right col., line 23). SAMs provide a stable monolayer from dilute solutions and ensuring a uniform immobilization (see e.g. pg. 45R, right col., lines 7-9).

The combine teaching of Choong et al. and Wink et al. are obvious over the instant claimed method because one of ordinary skill in the art would have been motivated to disclose sulfur containing self-assembled monolayer in the apparatus of Choong et al. for the advantage of providing a stable monolayer from dilute solutions and ensuring a uniform immobilization (Wink: pg. 45R, right col., lines 7-9). However, the combine teachings of Choong et al. and Wink et al. differ from the presently claimed invention by failing to include the substrate containing well structure and the shape and arrangement of the electrodes of claims 102, 121, and 122.

Weetall discloses a sensor apparatus for measuring the redox reaction occurring on the surface of the electrode array and the method for performing an immunoassay of an analyte on the sensor apparatus (see e.g. Abstract; col. 1, lines 8-12, and 46-68; claim 1).

The method comprises the steps of a) introducing into the well/sampling area the sample containing the analyte; b) applying a potential between the working electrode and counter electrode; c) measuring the current between the working electrode and counter electrode and

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determining the amount of analyte; and d) determining the amount of the analyte in the test sample from the measurement of the current in step (c) relative to the preselected potential in step (b) (see e.g. col. 1, lines 53-55; col. 2, col. 3, line 18 to col. 4, line 33; claim 1).

The sensor apparatus comprises a planar support with a plurality of wells (refers to instant claim 93) or with out wells, i.e. with define sampling area (see e.g. col. 2, lines 45-51; figs 3 and 4); each well/sampling area comprises a working electrode, counter electrode, and reference electrode; and an ammeter to control and monitor the electrodes in the wells/sampling area (see e.g. col. 1, lines 56-62; col. 2, lines 24-66; fig. 1-2, and 5; claim 1). Figures 3 and 4 disclose the arrangement of the electrodes on the support wherein the working electrode (ref. #22) is in the center and the counter electrode (ref. #26), and reference electrode (ref. # 24) is at the perimeter of the working electrode. The material for the support includes glass, and plastic polymer (see e.g. col. 2, lines 26-29). The electrodes are graphite electrodes (see e.g. col. 2, lines 38-42). The sample include biological sample and in liquid form (see e.g. col. 1, lines 63-68; col. 3, lines 4-13). Additionally, a sensor activating chemical attached to the working electrode that include a first conjugate wherein it is a specific binding partner to the analyte of interest (see e.g. col. 4, lines 55-60).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the substrate containing well structure and the shape and arrangement of the electrodes of claims 102, 121, and 122 as taught by Weetall in the apparatus of Choong et al. and Wink et al. One of ordinary skill in the art would have been motivated to include the substrate containing well structure and the shape and arrangement of the electrodes of claims 102, 121, and 122 in the apparatus of Choong et al. and Wink et al. because the shape and

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arrangement of the substrate and electrodes would be a choice of experimental design and is considered within the purview of the cited prior art. Moreover, both Choong et al. and include the substrate containing well structure and the shape and arrangement of the electrodes of claims 102, 121, and 122 disclose a biosensor comprising three electrode system (Choong: col. 5, lines 37-44; Weetall: col. 1, lines 56-62). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al., Wink et al., and Weetall because Weetall disclose by example the success of the apparatus that include the substrate containing well structure and the shape and arrangement of the electrodes of claims 102, 121, and 122.

Therefore, the combine teachings of Choong et al., Wink et al., and Weetall do render the apparatus and method of the instant claims *prima facie* obvious.

15. Claim 95 is rejected under 35 U.S.C. 103(a) as being unpatentable over Choong et al. (US Patent 6,518,024) in view of Wink et al. (*The Analyst*, **1997**, 122(4), pgs. 43R-50R) as applied to claims 83, 85-90, 94, 98-101, 103, 108, 112-118, 120, 123-125, and 129, and further in view of Han et al. (US Patent 6,268,161 B1).

Choong et al. disclose an apparatus and methods for detecting single base extension to an oligonucleotide using electrochemical redox labels (see e.g. Abstract; col. 1, lines 7-16; col. 3, lines 25-31; col. 9, lines 17-22).

The apparatus comprises a supporting substrate, a plurality of first electrode (refers to instant claimed working electrode), a counter electrode, and a reference electrode wherein the first electrode is in contact with a supporting substrate and oligonucleotide probes are

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immobilized on the first electrode via a polymer (see e.g. col. 5, line 15 thru col. 6, line 41; col. 7, lines 30-40). The substrate comprises materials such as silicon, glass, plastic, and ceramic (refers to instant claim 87) (see e.g. col. 5, lines 54-58). The substrate has a surface area of between $0.01 \mu\text{m}^2$ and 5 cm^2 (refers to instant claim 113)(see e.g. col. 6, lines 12-26). The first electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3). The counter electrode comprises materials such as gold, titanium, and platinum (refers to claims 89, 90, 101, and 118) (see e.g. col. 5, line 59 thru col. 6, line 3; col. 7, lines 29-40). The reference electrode comprises materials such as silver wire (refers to instant claimed limitation of “*the reference electrode consists of a single layer of an electrically conductive material*”, and claims 101 and 118). Additionally, the electrodes are connected to a power source and a means for controlling the power source.

The method comprises a) contacting the sample to the plurality of first electrodes, b) adding the reagent comprising the electrochemical redox labels, c) detecting the presence of the electrochemical redox labels to identify the base extension (see e.g. col. 4, lines 39-53; col. 8, lines 9-35; col. 10, lines 10-41). The detection step includes controlling the current flow between two electrodes (see e.g. col. 7, lines 41-50; col. 17-30). The detection method includes amperometric and cyclic voltammetry (refers to instant claims 114-117) (see e.g. col. 4, lines 5-14; col. 10, lines 10-41). In addition, Choong et al. disclose the step of forming the polymer onto the working electrode (see e.g. col. 11, lines 31-40).

Wink et al. disclose self-assembled monolayers (SAMs) and the methods of making and using the SAMs (see e.g. Abstract; pg. 43R, right col., lines 16-37). The class of monolayers includes disulfides (R-S-S-R), sulfides (R-S-R) and thiols (R-SH) that have a strong

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adsorption on a metal surface (see e.g. pg. 43R, right col., lines 26-29; pg. 44R, left col., lines 12-19). The SAMs modify sensor surface can be use in application such as electrochemical and surface plasmon resonance (see e.g. pg. 45R, right col., line 1 thru pg. 48R, left col., line 2). In electrochemical application, SAMs is use to immobilize biological molecules such as enzymes and DNA sequences (see e.g. pg. 46R, left col. line 5 thru right col., line 23). SAMs provide a stable monolayer from dilute solutions and ensuring a uniform immobilization (see e.g. pg. 45R, right col., lines 7-9).

The combine teaching of Choong et al. and Wink et al. are obvious over the instant claimed method because one of ordinary skill in the art would have been motivated to disclose sulfur containing self-assembled monolayer in the apparatus of Choong et al. for the advantage of providing a stable monolayer from dilute solutions and ensuring a uniform immobilization (Wink: pg. 45R, right col., lines 7-9). However, the combine teachings of Choong et al. and Wink et al. differ from the presently claimed invention by failing to include the calibration step comprising using two different calibration solutions.

Han et al. disclosed a biosensor for measuring the concentration of organic molecules in a solution (see e.g. col. 1, lines 16-17). Han et al. claim a method of using the biosensor that included a calibration step (see e.g. col. 12, lines 33-35; col. 16, claim 20). The claim method step includes a control solution (calibration solution) and obtaining a signal. Additionally, the system can be recalibrated by using a calibration solution with unknown amount of analyte (see e.g. col. 12, lines 60-62).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the calibration step comprising using two different calibration

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solutions as taught by Han et al. in the apparatus of Choong et al. and Wink et al. One of ordinary skill in the art would have been motivated to include the calibration step comprising using two different calibration solutions in the apparatus of Choong et al. and Wink et al. for the advantage of determining the performance of the electrode before the analysis of the sample (Han: col. 12, lines 34-36). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Choong et al., Wink et al., and Han et al. because the calibration step is necessary to ensuring the working order of the electrode.

Therefore, the combine teachings of Choong et al., Wink et al., and Han et al. do render the apparatus and method of the instant claims *prima facie* obvious.

Response to Arguments

16. Applicant's arguments and amendments, in which the limitation of '*the molecules in the self-assembly monolayer includes a sulfur that is bonded directly to the at least one electrode*' was added to claim 83, with respect to the all previous rejections of claims 83-95, 98-104, 108, 112-118, 120-127 have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, upon further consideration, new grounds of rejection are made in view of Wink et al. (*The Analyst*, 1997, 122(4), pgs. 43R-50R) regarding the newly added limitation of "*molecules in the self-assembly monolayer includes a sulfur that is bonded directly to the at least one electrode*".

17. Applicant's arguments with respect to the objection of claim 123 have been fully considered and are persuasive. The objection of claim 123 has been withdrawn. However, upon

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further reconsideration of claim 123 and the limitation of '*conducting an analysis of the sample that includes controlling a potential difference between the reference electrode and the working electrode... wherein the potential is controlled so as to cause a redox reaction between a component in the sample and the working electrode*' of claim 83, a new ground of objection is made.

Allowable Subject Matter

18. New claim 128 is objected to as being dependent upon a rejected base claim 83, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

My-Chau T. Tran
May 7, 2006

